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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/519,188	03/06/2000	Pancras C. Wong	PH-7038	8451

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EXAMINER

KIM, VICKIE Y

ART UNIT PAPER NUMBER

1614

DATE MAILED: 04/03/2003

18

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/519,188

Applicant(s)

WONG, PANCRAS C.

Examiner

Vickie Kim

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 17. 6) ☐ Other: .

DETAILED ACTION

Request for the Continued examination(RCE) acknowledged

1. The request filed on 12/18/2002 for a RCE under 37 CFR 1.114 based on parent Application No. 09/700,102 is acceptable and a RCE has been established. An action on the RCE follows.

Information Disclosure Statement

2. The information disclosure statement (IDS) submitted on March 18, 2003 was filed after the mailing date of the notice of allowance on Feb. 11, 2003. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Status of Application

3. Claim 1 is presented for the examination. The claim 1 is allowed based on the 131 declaration which is filed to antedate the priority date of Cariou's reference(AU698456-Pub. Date:10-29-1998). The deficiency was found in the declaration because the reference(CA2199642) cited has publication date of Sep. 10, 1998(see front page of the patent) . Thus, the 131 declaration is fail to antedate the priority date of the reference cited.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

1. Claim 1 is rejected under 35 U.S.C. 102(a) as being anticipated by Cariou et al (CA2199642, publication date:09/10/1998).

Claim 1 reads on a method of treating thrombosis in a mammal comprising administering a synergistic combination of a Factor Xa inhibitor and aspirin wherein the dose administered for at least one of a Factor Xa inhibitor and aspirin is a subtherapeutic dose to provide synergistic effect. The subtherapeutic dose in light of specification(see example 1 at page 20, lines 1-14) is exemplified such that the dose of aspirin is 1mg/kg or the dose of factor Xa is 0.1mg/kg. In applicant's own admission, the synergistic effect(see page 18) is most clearly demonstrated at suboptimal concentrations of the compounds. Cariou et al (CA'642) teach a use of a composition containing aspirin and a selective inhibitor of Factor Xa for treating thromboembolic diseases in a mammal, see abstract and claims 1 and 9-14. Cariou et al further teach an effective dose of the Factor Xa inhibitor or aspirin in said combination composition used in this treatment is 0.1 to 100mg per kilo of bodyweight, respectively. Cariou et al further teach that the treatment is successfully achieved by the combination of aspirin and a Factor Xa inhibitor via two different mechanisms of action(see page 3, lines 20-25). Thus, the claimed subject matter is taught by the cited reference and the recited limitations are met. It is noted that applicant admits that 0.1mg/kg of a factor Xa inhibitor or 1mg/kg of aspirin alone fails to show the therapeutic effectiveness(see at page 20, lines 3-5). Thus, the recited limitation(i.e. synergistic effect) is also inherently possessed

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when the successful treatment(i.e. treating thrombosis) is achieved by the patented composition comprising a combination of aspirin and a Factor Xa inhibitor at the suboptimal concentration of each component, for example, 0.1mg/kg of a Factor Xa inhibitor or 0.1-1mg/kg of aspirin, respectively. All the claims are anticipated and not patentably distinct over the prior art of the record.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Marlowe et al(WO 96/40744).

Wo'744 teaches a mammalian factor Xa inhibitor and its use in the treatment of thrombosis, see abstract and page 3, lines 25-30. It further teaches a beneficial combination drug therapy comprising factor Xa inhibitor(as patented) and aspirin (see page 36, lines 20-28) wherein the combination is advantageously used in the treatment of undesired thrombosis.

Applicant's claim differs because it requires synergistic combination which requires subtherapeutic dose of at least one component.

However, it would have been obvious to one of ordinary skill in the art that the minor variations including the selection of optimal dosages, routes of administration, or variable applications in order to determine the most effective

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treatment is well within the skilled level of artisan having ordinary skill in the art, and is obvious.

One would have been motivated to make such combination because aspirin is notoriously known in the art where abundant informations are available for therapeutic utility and safety. And it is also conventional wisdom that the most optimal treatment is successfully achieved by the combining two components utilizing different underlying mechanisms of action so that each component assists the other by different route where the combination improves the therapeutic effects while reducing effective dose which results in the reduction of unwanted side effects. The combination drug therapy is conventional knowledge and well within the skilled level of the artisan wherein one would have contemplated and titrated the most optimal dosage regimen, and expected reasonable success without undue experiment.

Conclusion

4. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vickie Kim whose telephone number is 703-305-1675. The examiner can normally be reached on Tuesday-Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel can be reached on 703-308-4725. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-3165 for regular communications and 703-746-3165 for After Final communications. Any inquiry of a general nature or relating to the status of this

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application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

A handwritten signature in black ink, appearing to read 'Vickie Kim', with a long horizontal flourish extending to the right.

Vickie Kim,
Patent examiner
March 28, 2003
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